

An Urgent Need for Local Guidelines to Address Phosphate Homeostasis in Children with Transfusion-dependent β -thalassemia Major

Sir,

The purpose of this communication is to alert the readers and other relevant stakeholders about a significant problem of a need of local guidelines on the management of metabolic bone disease (MBD) in children with β -thalassemia major (β -TM).

MBDs of multifactorial origin are frequently encountered in the children with β -TM. With a carrier frequency of 6-7% of β -thalassemia gene in the Pakistani population, around 5, 250 infants are born with β -TM annually. Yet, there is no national interest to address bone disorders in these patients. In the last decade, areas of vitamin D, calcium (Ca), and PTH homeostasis in patients with transfusion-dependent β -TM have been researched extensively. However, the effects on phosphate (PO_4) homeostasis are unclear.

Results from our unpublished pilot study revealed that 36.5% (n=134) of transfusion-dependent β -TM children (n=380; age range 5-17 years) had high-serum PO_4 levels (Median= 6.13 mg/dl with IQR of 7-5.7), findings consistent with the study by Tangngam *et al.*, which found asymptomatic hypoparathyroidism in 38% of the β -TM patients.¹ These patients also had significantly lower median plasma fibroblast growth factor-23 (FGF-23) levels than controls.¹ More studies on metabolic bone disease in children with β -TM by the Research Group at our institute show significant growth failure secondary to the iron overload with high-serum ferritin levels, denoting ineffective chelation.² High prevalence of bone pains and fragility fractures was significantly associated with hypovitaminosis D, hypocalcaemia, and hyperphosphatemia.³ Sultan *et al.* reported altered biochemical markers of bone turnover in regularly transfused thalassaemic patients, highlighting a direct correlation between serum PO_4 and ferritin levels. Both hypo- and hyperphosphatemia were seen in the patients.⁴ Similarly, in the population studied by Mirhosseini *et al.*, a high prevalence of hypocalcaemia (22%) and hyperphosphatemia (41.7%) suggested the incidence of asymptomatic hypoparathyroidism in patients with β -TM.⁵

Iron overload in β -TM contributes to low-circulating FGF-23 levels, leading to the high PO_4 loading. Physiologically, serum PO_4 is regulated by PTH, vitamin D, FGF-23, and its cofactor Klotho. FGF-23 reduces the formation of 1, 25-(OH)₂ D by inhibiting 1 alpha-hydroxylase, and as findings suggest, its impaired

response may disrupt PO_4 homeostasis that is furthering a vicious cycle of bone disease. We urge researchers to explore the relation among iron overload, FGF-23, and the Ca- PO_4 -PTH axis, so that we can develop local guidelines on the nutritional and pharmacological management of MBD in children with β -TM, which will help in lessening the economic burden of this life-altering disease.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

LJ, AHK: Idea conception, letter revision, and review.

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REFERENCES

1. Tangngam H, Mahachoklertwattana P, Poomthavorn P, Chuansumrit A, Sirachainan N, Chailurkit LO, *et al.* Under-recognised hypoparathyroidism in thalassemia. *J Clin Res Pediatr Endocrinol* 2018; **10(4)**:324. doi: 10.4274/jcrpe.0020.
2. Moiz B, Habib A, Sawani S, Raheem A, Hasan B, Gangwani M. Anthropometric measurements in children having transfusion-dependent beta thalassemia. *Hematol* 2018; **23(4)**:248-52. doi: 10.1080/10245332.2017.1396044.
3. Moiz B, Khan HA, Raheem A and Shariq M. High Prevalence of bone pain and fractures in young transfusion dependent patients with β -thalassemia at Southern Pakistan. *Ann Hematol Oncol* 2019; **6(2)**:1234.
4. Sultan S, Irfan SM, Ahmed SI. Biochemical markers of bone turnover in patients with β -thalassemia major: A single centre study from Southern Pakistan. *Adv Hematol* 2016; **2016**. doi: 10.1155/2016/5437609.
5. Mirhosseini NZ, Shahar S, Ghayour-Mobarhan M, Banihashem A, Kamaruddin NA, Hatef MR, *et al.* Bone-related complications of transfusion-dependent beta thalassemia among children and adolescents. *J Bone Miner Metab* 2013; **31(4)**:468-76. doi: 10.1007/s00774-013-0433-1.

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